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Response to Office Communication dated January 26, 2005

### REMARKS

As an initial matter, Applicants wish to thank the Examiner and his SPE for courtesies extended during the in person/telephonic interview of February 28, 2005. During the interview, the claim rejections and objections in the Office communication of January 26, 2005, were discussed. In that Office communication, Claims 1, 3, 5, 7-10, 14-20, 22-31, 38, 41 and 42 were rejected and an objection was directed towards claim 16.

Without prejudice or disclaimer, independent claim 1 is herein amended; claims 16 and 28 are canceled; and claims 5, 12, 13 and 43 are withdrawn as directed to non-elected species. With the entry of this amendment, claims 1, 3, 7-10, 14-15, 17-20, 22-27, 29-31, 38, 41 and 42 are pending. Applicants request reconsideration and allowance of the pending claims.

#### **Objection of Claim 16**

Claim 16 is rejected under 37 CFR 1.75 as allegedly being a substantive duplicate of claim 15. Action at page 3. Without prejudice or disclaimer and without acquiescence, Applicants have canceled claim 16. Applicants respectfully submit that the claim objection is rendered moot in light of this cancellation.

#### **Rejections Under 35 U.S.C. 112, first paragraph**

Claims 1, 3, 5, 7-10, 14-20, 22-31, 38, 41 and 42 are rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement. Action at page 3. Independent claim 1 is rejected as allegedly reciting matter not supported by the originally-filed specification and claims. Specifically, the phrases "to identify said phenotypic state with a disposable device" and "selling said disposable device" allegedly lacked written description support. Action at pages 4-5.

Without prejudice or disclaimer and without acquiescence to the Office's new matter characterization, Applicants have amended claim 1 as indicated in the Listing of Claims. Specifically, Applicants have cancelled the phrases "to identify said phenotypic state with a disposable device" and "selling said disposable device," obviating any issue of new matter.

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Claim 1 now recites "marketing diagnostic products that use said representative patterns wherein said diagnostic products are marketed with a disposable microfluidics device." Support for the amendment is found, e.g., in original claim 26, which provides "wherein said diagnostic products are marketed with a disposable microfluidics device." Thus there is no issue of new matter.

Claim 1 also now recites "identifying in a computer system representative patterns;" "the identity of a plurality of said more than 15 markers is not known" and "in a computer system identifying the differences in case samples and control samples using said plurality of said more than 15 markers".

Support for identifying in a computer system representative patterns can be found, e.g., at page 9, paragraph 0029, of the specification, which describes signal processing system and pattern recognition tools that extract information and classify patterns; as well as at page 18, paragraph 0070, which provides that output can be processed using a bio-informatics system, including a computer. Support for not knowing the identity of a plurality of markers can be found, e.g., at page 4, paragraph 0012, of the specification, reciting "without identification of some or all or the markers," which necessarily includes a plurality of the markers. Support for "in a computer system identifying the differences in case samples and control samples using said plurality of said more than 15 markers" can be found, e.g., at page 5, paragraph 0016, of the specification, describing that "bioinformatics systems are utilized to identify the differences in the polypeptide patterns in the case and control samples," where the collective profile is more important than the presence or absence of any specific entities. Support can also be found at page 4, paragraph 0013, describing how the business takes advantage of the presence of (or absence of) a pattern repeatedly found in the cases distinct from the controls, but the identity of some of the polypeptides is not known. Thus there is no issue of new matter with respect to the current claim 1 amendments.

Applicants respectfully request re-consideration and withdrawal of the 112, first paragraph, rejections of claim 1 and of pending claims 3, 7-10, 14, 15, 17-20, 22-27, 29-31, 38, 41 and 42 that depend (directly or indirectly) from claim 1.

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### **Rejections Under 35 U.S.C. 112, second paragraph**

Claims 1, 3, 5, 7-10, 14-20, 22-31, 38, 41 and 42 are rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Action at page 5. Applicants respectfully submit that the indefiniteness rejections are rendered moot in light of claim amendments and cancellations as detailed below:

#### **Claim 1**

Claim 1 is rejected for indefiniteness as "said spectral components" of claim 1 allegedly lacked antecedent basis. Action at page 6. Applicants have amended claim 1 to recite "mass spectral components" and to refer back to "said mass spectral components." Applicants respectfully submit there is no lack of antecedent basis in claim 1 as currently amended, and respectfully request re-consideration and withdrawal of the indefiniteness rejection of claim 1.

#### **Claim 5**

Claim 5 is rejected as indefinite for reciting "said kits" and depending from a claim that did not recite the word "kits." Action at page 6. Without prejudice or disclaimer, Applicants have withdrawn claim 5, as properly depending from withdrawn claim 4. Applicants reserve the right to consideration of claims to non-elected species upon allowance of a generic claim and preserve any rights to pursue claims to non-elected species in future continuing applications.

#### **Claim 28**

Claim 28 is rejected as indefinite with respect to the term "common protein." Action at page 6. Applicants have cancelled claim 28, without prejudice or disclaimer, rendering this rejection moot.

Applicants respectfully request re-consideration and withdrawal of the 112, second paragraph, rejections of claims 1, 5 and 28, as well as of pending claims 3, 7-10, 14, 15, 17-20, 22-27, 29-31, 38, 41 and 42, which depend (directly or indirectly) from claim 1.

### **Rejections Under 35 U.S.C. 102(a)**

Claims 1, 3, 7-10, 14-20, 22-24, 29-31, 38 and 42 are rejected as allegedly anticipated by Olek et al (US 2002/0137086). Action at page 7. Applicants have canceled claim 16, as

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noted above. With respect to the other claims rejected under 102(a), Applicants respectfully traverse.

As discussed during the interview, Applicants respectfully point out that Olek can not anticipate claim 1 as Olek fails to disclose certain limitation of the amended claim. Nor can Olek anticipate claims 3, 7-10, 14-15, 17-20, 22-24, 29-31, 38 and 42, which depend either directly or indirectly from claim 1.

**Anticipation rejection of claim 1 should be withdrawn as Olek fails to disclose at least 4 limitations of the amended claim**

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. Applicants respectfully point out at least three limitations of amended claim 1 that are not taught by the Olek reference.

*(1) Olek fails to teach the limitation for "without regard to a specific identity of at least some of said mass spectral components" of step (b)*

It is asserted that Olek "teaches determining relative amounts of protein relative to the expression level of at least one gene related to a genetic disease phenotype by gel electrophoresis followed by mass spectrometry" and refers to Olek paragraphs 0068, 0101, and 0102. Action at pages 7-8. However, without acquiescence, step (b) of claim 1 also recites "without regard to a specific identity of at least some of said mass spectral components." Olek fails to disclose or suggest that the specific identity of at least some mass spectral components, e.g., that may be obtained by gel electrophoresis followed by mass spectrometry, is not known. In contrast, the method of Olek requires specific identification of relevant markers. For example, Olek teaches developing gene panels by analyzing the expression level of at least one gene in at least one biological sample; selecting the gene(s) exhibiting a different expression level between at least two groups of biological material to develop a first knowledge base; and analyzing the level of cytosine methylation in the methylation relevant region of at least one gene selected on the basis of the first knowledge base. See Olek, paragraph 0060. Selecting one or more genes and determining their methylation levels presupposes identification of the gene, or else one would hardly know which gene to look at to determine its methylation state.

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Further, Olek provides that "a 'gene panel' designates a knowledge base, listing, table or other information source, that contains information about selected genes, herein also designated as 'candidate genes.'" Olek, paragraph 0089. Selected genes must have been identified to be compiled into such a gene panel. Moreover, Example 1 of Olek explains that "the resulting [mass spectrometry] fragments were analyzed via peptide mapping and compared to the protein database," confirming that selected markers are of known identity. Nowhere does Olek contemplate using mass spectral components where a specific identity of at least some of the mass spectral components would be disregarded. Accordingly, Applicants respectfully submit that claim 1, reciting the limitation "without regard to a specific identity of at least some of said mass spectral components," cannot be anticipated by Olek.

*(2) Olek fails to teach the limitation "the identity of a plurality of said more than 15 markers is not known" of step (c)*

According to the Office communication, Olek "teaches as examples of the disclosed invention applied to prostate cancer wherein the results of the above analysis can be further used in diagnosis and/or therapy as a minimal set of reliable markers" and it refers to Olek paragraph 0104. Action at page 8. However, without acquiescence, step (c) of claim 1 also recites "but the identity of a plurality of said more than 15 markers is not known." As detailed above, Olek fails to disclose or suggest not knowing the identity of some markers. Indeed, Olek does not contemplate an invention where the identities of a plurality of its "reliable markers" are not known. In contrast, Olek details that its gene panels "should not be understood as *merely* containing information about the names or designations of the candidate genes." Olek, paragraph 0089 (emphasis added). Where *mere* information about candidate genes involves their "names or designations," the identity of the candidates is clearly known and, accordingly, Olek cannot teach an invention where the identity of a plurality of markers is not known. Accordingly, Applicants again respectfully submit that amended claim 1 cannot be anticipated by Olek.

*(3) Olek fails to teach the limitation of "a disposable microfluidics device" of step (d)*

It is provided that Olek "teaches the use of a Genomic Solutions Flexys robotic as well as computer-based analysis software, such as Imagemaster from Amersham-Pharmacia and 'Z3' from Compugen, used in the diagnosis of prostate cancer" and that these devices are

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"clearly for sale, and are capable of being disposed of ... ." Action at page 8. Amended claim 1 step (d), however, recites "a disposable microfluidics device." Whether the Olek Flexys robotic and computer-based devices are disposable (in the sense that they can be disposed of), the devices are not microfluidics devices, as required in amended claim 1. Accordingly, Olek also fails to disclose or suggest "a disposable microfluidics device" and cannot anticipate amended claim 1.

*(4) Olek fails to teach the limitation of "in a computer system identifying the differences in case samples and control samples using said plurality of said more than 15 markers" of step (e)*

As discussed above and during the February 28, 2005, interview, Olek nowhere teaches using a plurality of markers of unknown identity to distinguish case and control samples, but rather requires specific identification of relevant markers e.g., genes that exhibit different methylation levels, and the development of gene panels for diagnosis of a disease. See Olek, paragraph 0090. Olek nowhere contemplates use of a computer system that identifies differences in case and control samples using a plurality of unidentified markers. Accordingly, Olek fails to disclose or suggest "in a computer system identifying the differences in case samples and control samples using said plurality of said more than 15 markers" where "said plurality" refers to the situation where "the identity of a plurality of said more than 15 markers is not known," as recited in amended claim 1, steps (c) and (e). Olek therefore cannot anticipate the claim, as amended.

For at least any one of the above reasons, Applicants respectfully request reconsideration and withdrawal of the 102(a) rejection of claim 1.

**Anticipation rejections of claims 3, 7-10, 14-15, 17-20, 22-24, 29-31, 38 and 42 should also be withdrawn as Olek fails to disclose at least 3 limitations of claim 1 from which the claims depend.**

Claims 3, 7-10, 14-15, 17-20, 22-24, 29-31, 38 and 42 each depend from claim 1, either directly (claims 3, 7, 14, 15, 22-24, 29-31, 38 and 42) or indirectly (claims 8, 9, 10, and 17-20). As noted above, the Olek reference fails to teach or suggest at least 4 limitations of amended claim 1, including "without regard to a specific identity of at least some of said mass spectral components," "the identity of a plurality of said more than 15 markers is not known," "a disposable microfluidics device," and "in a computer system identifying the

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differences in case samples and control samples using said plurality of said more than 15 markers." As claims 3, 7-10, 14-15, 17-20, 22-24, 29-31, 38 and 42 each depend from amended claim 1, they also cannot be anticipated by Olek. Accordingly, for at least this reason, Applicants respectfully request reconsideration and withdrawal of the 102(a) rejections with respect to claims 3, 7-10, 14-15, 17-20, 22-24, 29-31, 38 and 42.

#### **Common Ownership under 35 U.S.C. §103(c)**

Applicants wish to thank the Examiner for his reminder of the obligation to point out the inventor and invention dates of each claim in the case of a lack of common inventorship at the time a later invention was made. Applicants confirm that the inventors were each subject to an obligation of assignment to the same organization at the time of making the claimed inventions.

#### **Rejections under 35 U.S.C. §103(a)**

Claims 1, 3, 7-10, 14-20, 22-31, 38, 41 and 42 are rejected as obvious over Olek in view of Fouillet et al. (US 2001/0041357). Action at pages 10-12. As noted above, Applicants have cancelled claims 16 and 28. With respect to claims 1, 3, 7-10, 14, 15, 17-20, 22-27, 29-31, 38, 41 and 42, Applicants respectfully submit that the alleged combination does not render the claims obvious, as detailed below.

#### **Obvious rejection of claim 1 should be withdrawn as the Olek-Fouillet references fail to teach or suggest more than one limitation of the claim**

Claim 1 is rejected as obvious over Olek in view of Fouillet. Action at page 11. Applicants respectfully submit, however, that there is no *prima facie case* of obviousness because neither Olek nor Fouillet teaches or suggests a limitation of claim 1. M.P.E.P. 2142. Indeed, the Olek and Fouillet references fail to teach or suggest at least three limitations of claim 1.

As detailed above, the Olek reference fails to disclose the limitations of "without regard to a specific identity of at least some of said mass spectral components;" "the identity of a plurality of said more than 15 markers is not known;" and "in a computer system identifying the differences in case samples and control samples using said plurality of said more than 15 markers," each recited in amended claim 1. Fouillet does not cure this deficiency, either

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alone or in combination with Olek. Fouillet provides microfluidic devices having thermal transfer members that cycle between two or more temperatures, but nowhere teaches or suggests an invention where the identity of a plurality of mass spectral components or markers are not known or where a computer system identifies differences in case and control samples using the plurality of unidentified markers. As neither Olek nor Fouillet teaches or suggest these limitations, no combination of these two references can provide each and every limitation of claim 1.

Accordingly, at least for this reason, Applicants respectfully request reconsideration and withdrawal of the obviousness rejection directed at claim 1.

**Obvious rejection of claims 3, 7-10, 14, 15, 17-20, 22-27, 29-31, 38, 41 and 42 should be withdrawn as the Olek-Fouillet references fail to teach or suggest at least 3 limitations of the claim 1, from which the claims depend**

With respect to claims 3, 7-10, 14, 15, 17-20, 22-27, 29-31, 38, 41 and 42, Applicants respectfully submit that the obviousness rejections should be withdrawn as the Olek-Fouillet references fail to teach or suggest at least 3 limitations of claim 1, from which each of the claims depend either directly (3, 7, 14, 15, 22-25, 29-31, 38 and 42) or indirectly (8-10, 17-20, 26, 27 and 41).

As noted above, as neither Olek nor Fouillet teach or suggest at least 3 limitations of independent claim 1, no combination of these two references can provide each and every limitation of claim 1, required for a *prima facie* case of obviousness. As claims 3, 7-10, 14-15, 17-20, 22-27, 29-31, 38, 41 and 42 each depend from claim 1, they also cannot be rendered obvious by any combination of Olek and Fouillet. Accordingly, for at least this reason, Applicants respectfully request reconsideration and withdrawal of the 103(a) rejections directed at claims 3, 7-10, 14, 15, 17-20, 22-27, 29-31, 38, 41, and 42.

Finally, Applicants do not address the Office's further arguments applying certain disclosures of Olek and/or Fouillet to other elements and limitations of the claims. However, in doing so, Applicants in no way acquiesce to any of the Office's contentions.



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**CONCLUSION**

Applicants submit that the instant application is in condition for allowance and earnestly and respectfully request allowance of the now pending claims. Should the Examiner have any questions, the Examiner is invited and encouraged to contact the undersigned attorney at the direct number provided.

The Commissioner is authorized to charge any fees that may be required in connection with this submission, including petition fees and extension of time fees, and to credit any overpayments to Deposit Account No. 23-2415 (Attorney Docket No. 29191-707).

WILSON SONSINI GOODRICH & ROSATI

Respectfully submitted,

Date: 3/18/05

By: Nicole Fortune  
Nicole M. Fortuné  
Registration No. 52,905

650 Page Mill Road  
Palo Alto, CA 94304-1505  
Phone: (650) 493-9300  
Direct: (650) 849-3253  
Client No. 021971